National Toxicology Program
Toxicity Report Series
Number 69

NTP Technical Report on the Toxicity Studies of

Butanal Oxime

(CAS No. 110-69-0)

Administered in Drinking Water and by Gavage to F344/N Rats and B6C3F$_1$ Mice

January 2004

U.S. Department of Health and Human Services
Public Health Service
National Institutes of Health

FOREWORD

The National Toxicology Program (NTP) is made up of four charter agencies of the U.S. Department of Health and Human Services (DHHS): the National Cancer Institute (NCI), National Institutes of Health; the National Institute of Environmental Health Sciences (NIEHS), National Institutes of Health; the National Center for Toxicological Research (NCTR), Food and Drug Administration; and the National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control and Prevention. In July 1981, the Carcinogenesis Bioassay Testing Program, NCI, was transferred to the NIEHS. The NTP coordinates the relevant programs, staff, and resources from these Public Health Service agencies relating to basic and applied research and to biological assay development and validation.

The NTP develops, evaluates, and disseminates scientific information about potentially toxic and hazardous chemicals. This knowledge is used for protecting the health of the American people and for the primary prevention of disease.

The studies described in this Toxicity Study Report were performed under the direction of the NIEHS and were conducted in compliance with NTP laboratory health and safety requirements and must meet or exceed all applicable federal, state, and local health and safety regulations. Animal care and use were in accordance with the Public Health Service Policy on Humane Care and Use of Animals.

These studies are designed and conducted to characterize and evaluate the toxicologic potential of selected chemicals in laboratory animals (usually two species, rats and mice). Chemicals selected for NTP toxicology studies are chosen primarily on the bases of human exposure, level of production, and chemical structure. The interpretive conclusions presented in this Toxicity Study Report are based only on the results of these NTP studies. Extrapolation of these results to other species and quantitative risk analyses for humans require wider analyses beyond the purview of these studies. Selection *per se* is not an indicator of a chemical's toxic potential.

Details about ongoing and completed NTP studies are available at the NTP's World Wide Web site: http://ntp-server.niehs.nih.gov. Abstracts of all NTP Toxicity Study Reports and full versions of the most recent reports and other publications are available from the NIEHS' Environmental Health Perspectives (EHP) http://ehp.niehs.nih.gov (866-541-3841 or 919-653-2590). In addition, printed copies of these reports are available from EHP as supplies last. A listing of all the NTP Toxicity Reports printed since 1991 appears at the end of this Toxicity Report.

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PEER REVIEW

The draft report on the toxicity studies of butanal oxime was evaluated by the reviewers listed below. These reviewers serve as independent scientists, not as representatives of any institution, company, or governmental agency. In this capacity, reviewers determine if the design and conditions of these NTP studies are appropriate and ensure that the Toxicity Study Report presents the experimental results and conclusions fully and clearly.

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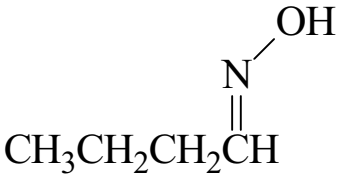
ABSTRACT



BUTANAL OXIME

CAS No. 110-69-0

Chemical Formula: C_4H_9NO Molecular Weight: 87.12

Synonyms: Butanaloxime; butylaldoxime; butyraldehyde oxime; *n*-butyraldehyde oxime; butyraldoxime; *n*-butyraldoxime
Trade names: Exkin 1, Exkin No. 1 Anti-Skinning Agent, Skino #1, Troykyd Anti-Skin BTO

Butanal oxime is used as a volatile antiskinning agent in paints, inks, and similar products. Butanal oxime was chosen for toxicology testing as a representative of the aldoxime class. Male and female F344/N rats and B6C3F$_1$ mice received butanal oxime (99% pure) in drinking water for 15 days or by gavage in 0.5% methylcellulose for 14 weeks. Animals were evaluated for clinical pathology, reproductive system effects, and histopathology. Genetic toxicology studies were conducted in *Salmonella typhimurium,* cultured Chinese hamster ovary cells, and mouse peripheral blood erythrocytes.

In the 15-day studies, groups of five male and five female rats and mice received 0, 312, 625, 1,250, 2,500, or 5,000 ppm butanal oxime in drinking water, resulting in average daily doses of approximately 40, 70, or 100 mg butanal oxime/kg body weight to male and female rats; 45, 90, 130, 200, or 300 mg/kg to male mice; and 45, 85, 100, 130, or 170 mg/kg to female mice. Due to body weight loss and lack of water consumption, all male and female rats receiving 2,500 or 5,000 ppm were removed from the study on day 9; average daily doses were not calculated for these groups. All other rats and mice survived until the end of the studies. Mean body weights of 1,250 ppm male and female rats and 2,500 and 5,000 ppm male and female mice were significantly less than those of the controls. Male mice receiving 5,000 ppm and females receiving 2,500 or 5,000 ppm lost weight during the study. Water consumption by rats and mice receiving 1,250 ppm or greater was less than that by the controls. Thinness in

2,500 and 5,000 ppm rats and mice was the only clinical finding of toxicity. Spleen weights were significantly decreased in 2,500 and 5,000 ppm female mice. No chemical-related lesions were observed grossly; histologic examinations were not performed.

In the 14-week studies, groups of 10 male and 10 female rats and mice received butanal oxime by gavage at doses of 0, 25, 50, 100, 200, or 600 mg/kg, 5 days per week for 14 weeks. All 600 mg/kg rats died or were killed moribund during the first week of the study; in the 600 mg/kg mouse groups, seven males and nine females died, were killed moribund, or were killed accidentally before the end of the study. Mean body weights of 100 and 200 mg/kg male rats, 600 mg/kg male mice, and female mice administered 50 mg/kg or greater were less than those of the controls. Clinical findings of toxicity in 600 mg/kg rats included loss of coordination, wobbly gait, shaking, blinking, constant grooming and scratching of the face, head weaving, burying of the face in bedding, lethargy, and prostration; in 600 mg/kg mice, clinical findings included ataxia, loss of balance after rearing, squinting, and burying of the face in the bedding.

Hematology results of the 14-week gavage studies indicate that butanal oxime induces a methemoglobinemia and a responsive anemia in rats and mice.

Spleen weights of 100 and 200 mg/kg male rats, female rats administered 50 mg/kg or greater, and 200 and 600 mg/kg male mice were increased, as were the liver weights of 200 mg/kg female rats and mice.

In animals that died early due to butanal oxime administration, hepatocellular necrosis was the primary pathologic finding. Degeneration of the nasal olfactory epithelium was observed in dosed rats and mice that died early as well as in animals that survived to the end of the studies. Additional chemical-related nasal findings were respiratory epithelial changes in male rats and suppurative exudate in male and female mice. Increased incidences and/or severities of splenic hematopoietic cell proliferation and pigmentation (hemosiderin) as well as bone marrow hyperplasia were also observed in dosed groups, particularly in the 200 and 600 mg/kg groups, and were indicative of erythrocyte damage.

Butanal oxime (3 to 10,000 µg/plate) was mutagenic in *S. typhimurium* strain TA1535 in the presence of 5% or 10% rat liver S9; an equivocal response was seen in TA100 with 30% rat S9, and no mutagenic activity was seen in TA98, with or without rat or hamster liver S9. Butanal oxime induced chromosomal aberrations in cultured Chinese hamster ovary cells, with and without S9. Significant increases in the frequencies of micronucleated normochromatic erythrocytes were observed *in vivo* in peripheral blood of male and female mice administered 25 to 600 mg/kg butanal oxime for 14 weeks by gavage.